JACC Vol. 15, No. 3
March 1, 1990:658–64

Alterations in Left Ventricular Relaxation During Atrioventricular Pacing in Humans

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To determine whether the asynchronous left ventricular contraction-relaxation sequence that exists during right ventricular pacing alters left ventricular relaxation, measurements of both the maximal rate of decline of left ventricular pressure (peak negative dP/dt) and the time constant of left ventricular relaxation were obtained during atrial and atrioventricular (AV) pacing in 25 patients referred for diagnostic cardiac catheterization. Heart rate was maintained at 10 to 15 beats/min above the sinus rate at rest, and relaxation was assessed during atrial pacing, AV pacing and repeat atrial pacing.

The patients were classified into two groups. Group 1 included 10 patients with normal left ventricular systolic function at rest (ejection fraction >0.55) and without evidence of prior myocardial infarction. Group 2 included 15 patients with a depressed left ventricular ejection fraction or akinesia of one or more left ventricular segments on the contrast ventriculogram, or both. Heart rate, peak left ventricular systolic pressure, end-systolic pressure and end-diastolic pressure remained constant during atrial, AV pacing and repeat atrial pacing in all patients.

In group 1 patients, the decrease in peak negative dP/dt (1,507 ± 200 versus 1,424 ± 187 mm Hg/s) and the increase in the time constant of left ventricular relaxation (48 ± 11 versus 51 ± 11 ms) during AV pacing was not significantly different when compared with values during atrial pacing. In group 2 patients, peak negative dP/dt decreased from 1,358 ± 333 during atrial pacing to 1,222 ± 240 mm Hg/s ($p < 0.0005$) during AV pacing, and the time constant of left ventricular relaxation increased from 59 ± 8 to 71 ± 15 ms ($p < 0.0001$). Maximal rate of rise of left ventricular pressure (peak positive dP/dt) also decreased during AV pacing in patients in group 1 (1,499 ± 310 to 1,381 ± 261 mm Hg/s; $p < 0.0005$) and group 2 (1,385 ± 271 to 1,233 ± 231 mm Hg/s; $p < 0.0005$).

These results suggest that the asynchronous contraction-relaxation sequence that occurs during right ventricular pacing alters left ventricular relaxation in patients with abnormal left ventricular systolic function.

(J Am Coll Cardiol 1990;15:658–64)

Myocardial relaxation is an energy-dependent process in which cytosolic calcium is returned to the sarcoplasmic reticulum (1,2). This adenosine triphosphate (ATP)-dependent reuptake process separates calcium from troponin, inhibiting the interaction of actin and myosin and resulting in cross-bridge detachment and myocardial relaxation (3).

Physiologic measurements that describe early diastole include the rate of decline in left ventricular pressure (peak negative dP/dt) and the duration of the isovolumetric relaxation period. The most widely used and extensively studied index (4–6) is the time constant of relaxation, which is derived from a monoexponential analysis of the decay in left ventricular pressure during the isovolumetric portion of diastole. A variety of conditions that alter the systolic performance of the left ventricle also prolong myocardial relaxation (7). These include coronary artery disease, hypertensive heart disease, congestive and hypertrophic cardiomyopathy and valvular heart disease (8,9). In addition, disease processes that produce asynchronous or nonuniform left ventricular contraction and relaxation also influence the ability of the left ventricle to relax (8–10).

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Manuscript received July 18, 1989; revised manuscript received October 4, 1989, manuscript accepted October 10, 1989.

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0735-1097/90/$3.50

Atrioventricular (AV) sequential pacing from the right atrium and right ventricle produces prolongation of the QRS complex and a left bundle branch block configuration on the electrocardiogram (ECG). This pattern of depolarization and repolarization creates asynchrony in left ventricular contraction and relaxation in animals (11–15). To determine whether the inhomogeneous left ventricular contraction-relaxation sequence that occurs during right ventricular pacing alters left ventricular relaxation in humans, we measured both peak negative dP/dt and the time constant of relaxation during temporary atrial and AV sequential pacing under conditions in which heart rate and load remained constant.

Methods

Study patients. This study was performed prospectively over a 2 month period and included 25 patients referred for elective cardiac catheterization for the evaluation of chest pain. Only patients without congestive heart failure, valvular heart disease, unstable angina or underlying left bundle branch block on the resting ECG were asked to participate in the study. Written, informed consent was obtained from all patients.

The patients were classified into two groups on the basis of results of the contrast ventriculogram. Group 1 included 10 patients with normal left ventricular systolic function at rest (ejection fraction >0.55) and normal regional wall motion on the contrast ventriculogram. Group 2 included 15 patients with depressed global systolic function (ejection fraction <0.55) or an abnormality of one or more left ventricular segments on the contrast ventriculogram, or both. All patients were premedicated with oral diphenhydramine (25 to 50 mg) and chlordiazepoxide (25 to 50 mg) 1 h before the study. Antianginal medications were not withheld during the study and included nitrates (n = 19), calcium channel antagonists (n = 18) and beta-adrenergic blocking agents (n = 13).

Study protocol. Two 6F bipolar pacing catheters (Electro-Catheter) were introduced by way of the femoral vein and positioned in the right atrium and right ventricular apex under fluoroscopic guidance. The longest AV interval (126 ± 21 ms) producing a right ventricular activation sequence (left bundle branch block) was chosen to maximize the hemodynamic benefit of atrial contraction. A 7F micromanometer catheter (Millar Instruments) was then advanced to the left ventricle from the femoral artery. High fidelity left ventricular pressure tracings were recorded at a paper speed of 100 mm/s on a physiologic recorder (VP-16, Honeywell). In addition, on-line left ventricular pressure was digitized for 50 to 60 consecutive beats at a frequency of 200 Hz with an analog to digital converter interfaced to an IBM AT computer. Left ventricular systolic and end-diastolic pressure, end-systolic pressure (pressure at maximal negative dP/dt), peak positive and negative dP/dt and the time constant of left ventricular relaxation were obtained from the digitized left ventricular pressure tracings with use of the computer analysis to be described.

When all catheters were in place, atrial pacing was initiated at a rate approximately 10 beats/min above the sinus rate at rest. After 3 min, heart rate and left ventricular pressure were measured. Atrioventricular sequential pacing using the same atrial rate and the previously determined AV interval was then initiated, and after 3 min hemodynamic measurements were recorded. Atrial pacing was then repeated after termination of ventricular pacing and hemodynamic measurements were again recorded. Because a period of repeat atrial pacing was not initially included in the protocol, repeat measurements are not available for the first three patients. All hemodynamic measurements were made before the injection of radiographic contrast agents, and the reported values represent the average of 20 to 50 beats. Premature and postpremature ventricular beats were excluded from analysis.

Computer analysis of left ventricular pressure. The decay of left ventricular pressure with time can be closely approximated by the exponential relation:

$$P = P_0 e^{-at} + P_B, \quad [1]$$

where P is left ventricular pressure, P_0 is pressure at peak negative dP/dt, t is the time in milliseconds after peak negative dP/dt, P_B is the left ventricular asymptotic pressure assuming that left ventricular pressure decays to infinity and a is the constant of the exponential relation (5,6). The first derivative of this equation with respect to t is the following:

$$dP/dt = -aP_0 e^{-at}. \quad [2]$$

If $P - P_B$ is then substituted from the first equation to eliminate $P_0 e^{-at}$, the equation becomes the following:

$$dP/dt = -a(P - P_B). \quad [3]$$

To derive the time constant of relaxation (T), the computer identified 15 to 20 points on the pressure decay curve between maximal negative dP/dt and left ventricular end-diastolic pressure (4,6,16). The resulting values were then fit by equation 3 and the constant a was calculated by the method of least squares (mean correlation coefficient 0.991 ± 0.005); $T = -1/a$.

Two-dimensional echocardiography. Two-dimensional echocardiographic examination was obtained 18 ± 27 days from the time of cardiac catheterization to accurately measure left ventricular wall thickness. Echocardiographic recordings were performed by an experienced operator using a commercially available instrument (VingMed CFM 700). All subjects were studied in the supine or partial left lateral

Table 1. Clinical Characteristics of 25 Patients

	Group 1 (n = 10)	Group 2 (n = 15)	p Value
Age (yr)	59 ± 10	55 ± 10	NS
LV ejection fraction	0.68 ± 0.08	0.47 ± 0.08	0.0001
LV end-diastolic volume (ml/m^2)	69 ± 12	100 ± 49	0.07
LV end-systolic volume (ml/m^2)	22 ± 6	51 ± 21	0.0004
QRS duration (ms)	85 ± 15	76 ± 4	NS
Wall thickness (cm)	1.11 ± 0.14	1.22 ± 0.28	NS
No. of diseased coronary vessels per patient	2.2 ± 1.2	2.3 ± 0.9	NS
No. of patients taking calcium channel antagonists	7	11	NS
No. of patients taking beta-adrenergic blocking agents	5	8	NS
No. of patients taking nitrates	6	13	NS

Values are expressed as mean values ± 1 SD. LV = left ventricular; NS = not significant.

decubitus position with use of a 3.5 MHz imaging transducer. Standard echocardiographic measurements of left ventricular end-diastolic wall thicknesses were performed in the short-axis view at the level of the papillary muscles.

Angiographic analysis. After hemodynamic measurements were obtained, coronary angiography and biplane ventriculography were performed. Significant coronary artery disease was defined as the presence of >50% luminal narrowing in any major epicardial vessel. Left ventricular volumes were determined with the area-length method (17).

Statistical methods. All data are expressed as mean values ± 1 SD. Two-way analysis of variance for repeated measures was used to compare the effects of atrial, AV sequential and repeat atrial pacing. A two-tailed Student's *t* test with Bonferroni adjustment was used for comparisons between groups 1 and 2 for continuous variables and a chi-square analysis for discrete variables. A p value ≤0.025 was considered significant. Linear regression analysis was used to identify variables that correlated with the percent change in isovolumetric relaxation time.

Results

Clinical characteristics (Table 1). All 10 patients in group 1 had a normal left ventricular ejection fraction and had normal left ventricular end-diastolic and end-systolic volumes. Compared with group 1 patients, the 15 group 2 patients had diminished left ventricular systolic function with depressed ejection fraction ($p < 0.0001$) and increased left ventricular end-systolic volume ($p < 0.0004$). There were no differences between group 1 and group 2 patients in the number of diseased coronary vessels or ventricular wall thickness or in the number of patients receiving calcium channel antagonists, beta-adrenergic blocking drugs or long-acting nitrates.

There were no differences between group 1 and group 2 in baseline systolic blood pressure, end-systolic pressure, end-diastolic pressure, heart rate, peak positive and negative dP/dt or QRS duration. Baseline time constant of ventricular relaxation was prolonged in the group 2 patients when compared with values in group 1 patients (59 ± 8 versus 48 ± 11 ms, $p < 0.01$).

Table 2. Hemodynamic Effects of Atrial, AV Sequential and Repeat Atrial Pacing in 25 Patients

	Group 1 (n = 10)			Group 2 (n = 15)		
	Atrial Pacing	AV Pacing	Rep. Atrial Pacing	Atrial Pacing	AV Pacing	Rep. Atrial Pacing
Heart rate (beats/min)	84 ± 9	84 ± 9	85 ± 10	83 ± 7	83 ± 7	83 ± 7
LV SP (mm Hg)	116 ± 13	115 ± 13	118 ± 17	121 ± 30	121 ± 30	124 ± 33
LV ESP (mm Hg)	70 ± 10	69 ± 10	70 ± 13	72 ± 19	73 ± 20	73 ± 19
LV EDP (mm Hg)	10 ± 3	10 ± 2	10 ± 3	10 ± 4	10 ± 4	10 ± 5
+dP/dt (mm Hg/s)	1,499 ± 310	1,381 ± 261*	1,531 ± 309	1,385 ± 271	1,233 ± 231*	1,400 ± 285
T (ms)	48 ± 11	51 ± 11	49 ± 10	59 ± 8	71 ± 15†	60 ± 8
−dP/dt (mm Hg/s)	1,507 ± 200	1,424 ± 187	1,517 ± 227	1,358 ± 333	1,222 ± 240*	1,369 ± 328

*$p < 0.0005$ compared with atrial pacing; †$p < 0.0001$ compared with atrial pacing. All values are expressed as mean values ± 1 SD. AV = atrioventricular; +dP/dt = maximal rate of rise in left ventricular pressure; −dP/dt = maximal rate of decline in left ventricular pressure; EDP = end-diastolic pressure; ESP = end-systolic pressure; LV = left ventricular; Rep. = repeat; SP = systolic pressure; T = isovolumetric relaxation time.

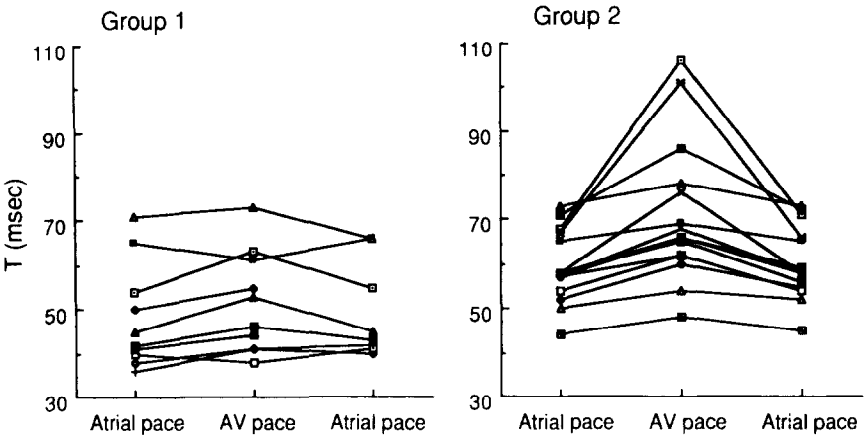

Figure 1. Plot of the time constant (in milliseconds) of isovolumetric relaxation (T) during atrial, atrioventricular (AV) and repeat atrial pacing (pace) in patients in group 1 (normal systolic function) and group 2 (systolic dysfunction).

Hemodynamic effects of atrial and AV sequential pacing (Table 2). Heart rate, end-systolic pressure and peak left ventricular systolic and end-diastolic pressures remained constant during atrial and AV sequential pacing in both patient groups. During AV sequential pacing, there was a prolongation in the QRS complex from 80 ± 14 to 133 ± 20 ms ($p < 0.0001$) and a decrease in peak positive dP/dt in both group 1 ($p < 0.0005$) and group 2 ($p < 0.0005$) patients.

Effects of AV sequential pacing on diastolic function. The changes in maximal negative dP/dt and isovolumetric relaxation time (T) during atrial and AV sequential pacing are shown in Table 2 and Figure 1. In group 1 patients, neither maximal negative dP/dt nor isovolumetric relaxation time was significantly changed during AV sequential pacing when compared with values during atrial pacing. In group 2 patients, atrioventricular sequential pacing produced a decrease in maximal negative dP/dt ($p < 0.0005$) and an increase in isovolumetric relaxation time ($p < 0.0001$) when compared with values during atrial pacing. The increase in isovolumetric relaxation time, expressed as both absolute change and percent change, was greater in group 2 patients when compared with group 1 patients ($p < 0.01$). All values returned to baseline when atrial pacing was repeated 3 min after the termination of AV sequential pacing.

Discussion

This study demonstrates that right ventricular pacing further prolongs left ventricular relaxation in patients with preexisting left ventricular systolic dysfunction.

Background on contraction-relaxation asynchrony. In the intact heart, abnormalities producing contraction-relaxation asynchrony result from interactions between spatially disparate myocardial segments (10–15). Myocardial fiber shortening may occur in one region of the heart while lengthening occurs in another segment (14,15). This abnormal relaxation sequence inhibits the ability of the left ventricle to relax normally (11–15). Asynchronous left ventricular contraction and relaxation may be seen in a variety of human disease processes, such as ischemia, infarction and bundle branch block, all of which produce an abnormally prolonged isovolumetric relaxation period (8–10).

Ventricular pacing stimulates initial electrical and mechanical activation in the area of the myocardium closest to the intracardiac electrode, while remote areas become activated as depolarization spreads through the myocardium (10–15). Thus, a functionally inhomogeneous contraction-relaxation sequence is created that may adversely affect the ability of the left ventricle to relax.

Effect of ventricular pacing on left ventricular function. To determine whether the asynchronous contraction-relaxation sequence induced by pacing from the right ventricle altered left ventricular relaxation, we measured both the rate of isovolumetric pressure decay and maximal negative dP/dt during atrial and AV sequential pacing. In patients with abnormal baseline systolic function, both indexes of myocardial relaxation worsened during AV sequential pacing.

In addition to the effect on diastolic function, maximal dP/dt was also decreased during AV sequential pacing. These results, confirmed in earlier studies, are further supported by the recent finding (12–14,18) that the slope of the end-systolic pressure-volume relation is reduced during AV sequential pacing in humans. Because isovolumetric relaxation is sensitive to changes in the inotropic state of the heart (6,11), it is conceivable that the change in systolic function during AV sequential pacing produced the observed changes in diastolic function. However, peak positive dP/dt decreased similarly in both group 1 and group 2 patients during AV sequential pacing, although isovolumetric relaxation time prolonged and peak negative dP/dt decreased only in patients with baseline left ventricular dysfunction. This finding suggests that the observed impairment in left ventricular relaxation occurred independent of the changes in systolic function. Thus, a decrease in peak positive and negative dP/dt and an increase in the time constant of

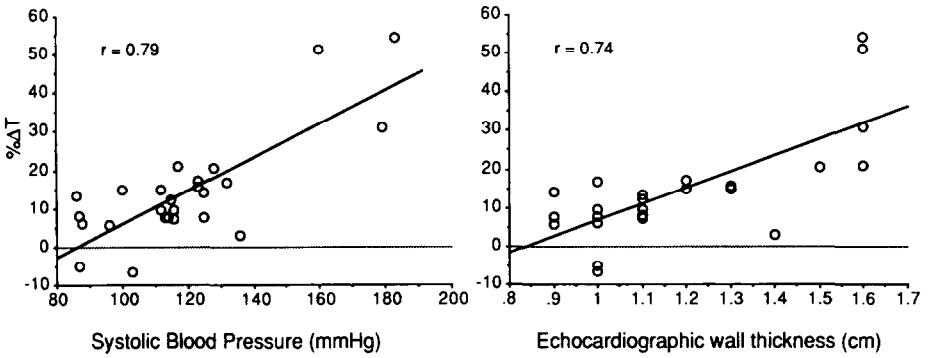

Figure 2. Linear regression plots comparing systolic blood pressure (**left panel**) and echocardiographic wall thickness (**right panel**) with the percent change in the time constant of isovolumetric relaxation (%ΔT).

isovolumetric relaxation while preload, afterload and heart rate remained constant suggests impairment of myocardial contraction and relaxation.

The time constant of isovolumetric relaxation increased during AV sequential pacing in all but two patients (Fig. 1). It is also evident that some patients had a more marked prolongation in the time constant of isovolumetric relaxation during AV sequential pacing. Clinical and hemodynamic characteristics, such as baseline isovolumetric relaxation time, ejection fraction, ventricular volumes, end-diastolic pressure or antianginal therapy did not predict the degree to which isovolumetric relaxation time (T) prolonged during AV sequential pacing. There was, however, a close correlation between peak systolic pressure (r = 0.79) and left ventricular wall thickness (r = 0.74) measured by two-dimensional echocardiography and the percent increase in T (Fig. 2). It is conceivable that in patients with an increased myocardial mass, electrical depolarization propagates more slowly through the thickened myocardium, thus delaying mechanical activation and producing a more markedly asynchronous contraction-relaxation sequence. This view is further supported by a correlation between the duration of the QRS complex during AV pacing and the percent change in isovolumetric relaxation time (r = 0.59).

Earlier studies. The hemodynamic effects of cardiac pacing have been well documented (19–24). During ventricular pacing, loss of atrial contraction or a ventriculoatrial activation sequence may produce a decrease in systemic blood pressure and cardiac output with a concomitant rise in both atrial and pulmonary artery pressures (21,22). The return of atrial synchrony during AV sequential pacing produces both acute and sustained hemodynamic improvement (21,22) although the asynchronous contraction-relaxation sequence that remains has a depressant effect on systolic function (18,25–28). Previous animal studies (29–31) suggest that endocardial pacing from different sites in the right or left ventricle may influence the strength of left ventricular contraction. Wiggers (32) originally proposed that the more muscle activated before excitation of the Purkinje system, the greater the asynchrony and the weaker the resulting contraction . The present investigation clearly demonstrates that AV sequential pacing has a depressant effect on diastolic function as well. Thus, both systolic and diastolic left ventricular performance are optimized by conduction through a normal AV node (18,25–31).

Clinical implications. Of the 235,000 permanent pacemakers implanted worldwide in 1986, 40% to 50% were for patients with symptomatic sinus node disease (33,34). If AV node conduction is normal, permanent atrial pacemaker implantation has been shown to be safe and may have a beneficial effect on long-term survival when compared with ventricular pacing (33,35–37). Current trends in permanent pacemaker implantation, however, suggest that dual chamber or ventricular pacemakers are often substituted under these circumstances (33,34). Our data suggest that patients with depressed systolic function and intact AV node conduction may benefit hemodynamically from either single chamber atrial pacing or from programming an appropriate AV delay to avoid ventricular pacing if a dual chamber device is used.

Limitations. Earlier investigations (38) have suggested that a monoexponential analysis of left ventricular pressure decay may not be possible in the presence of gross asynchrony, whereas others (39) have recently demonstrated that during nonuniform left ventricular contraction and relaxation, the time constant of left ventricular relaxation accurately reflects important changes in left ventricular relaxation. Analysis of the suitability of the monoexponential model during AV sequential pacing is illustrated by Figure 3. A plot of negative-dP/dt versus left ventricular pressure and the corresponding plot of left ventricular pressure versus time for one cardiac cycle clearly demonstrate the linear relation of isovolumetric relaxation and the suitability of the monoexponential model during AV sequential pacing (38). This plot illustrates data obtained from the patient with the greatest changes in time constant of relaxation and negative dP/dt and is representative of the other patients in the study. In addition, peak negative dP/dt, which is not dependent on a monoexponential analysis, changed in the same direction as the time constant of relaxation in all patients.

The importance of an appropriate AV delay on ventricular performance has been well documented (20,21). It may

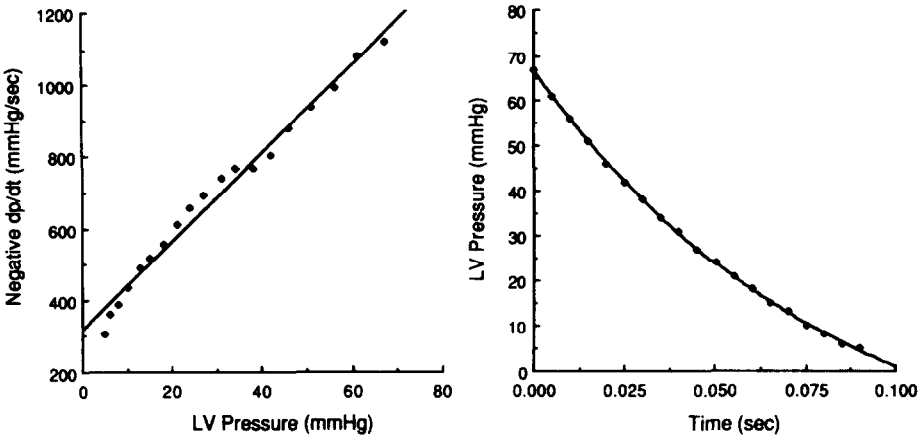

Figure 3. Left panel, Plot of left ventricular (LV) pressure compared with maximal rate of decline of left ventricular pressure (negative dP/dt) during isovolumetric relaxation for a single cardiac cycle during atrioventricular (AV) pacing. **Right panel**, Plot of time compared with left ventricular pressure during isovolumetric relaxation for a single cardiac cycle during AV pacing. **Left and right panels** represent data obtained from the same cardiac cycle.

be argued that the shortened AV interval used in this study could account for the demonstrated effects on diastolic function. However, during AV sequential pacing, left ventricular systolic pressure and left ventricular filling as measured by end-diastolic pressure were unchanged. This finding suggests that the observed changes are not due to hemodynamic alterations but reflect a change in left ventricular relaxation. Additionally, the measured indexes of diastolic function reflect changes that occur during the isovolumetric period of relaxation. The methods used in this study do not allow evaluation of the effect of AV sequential pacing on passive diastolic filling. Recent studies (13) have shown that in addition to impaired relaxation, passive diastolic filling is also abnormal during AV sequential pacing.

We express our appreciation to Chuck Hougland for expert technical assistance. We also express our appreciation to Arvella Peters for help in performing the echocardiograms and Donald Haagen, RCPT, Janie McCoulskey, CCRN, Willie Gary, Graciella Fields, Jenelle Durbin, RN and Barbara Hatfield, RN for help in performing the hemodynamic studies.

References

1. Carafoli E. The homeostasis of calcium in heart cells. J Mol Cell Cardiol 1985;17:203–12.
2. Katz AM. Sarcoplasmic reticular control of cardiac contraction and relaxation. In: Grossman W, Lorell BH, eds. Diastolic Relaxation of the Heart. Boston: Martinus Nijhoff, 1988:11–5.
3. Brutsaert DL, Housmans PR, Goethals MA. Dual control of relaxation: its role in ventricular function in the mammalian heart. Circ Res 1980;47: 637–52.
4. Weiss JL, Frederiksen JW, Weisfeldt ML. Hemodynamic determinants of the time-course of fall in canine left ventricular pressure. J Clin Invest 1976;58:751–60.
5. Raff GL, Glantz SA. Volume loading slows left ventricular isovolumic relaxation rate: evidence of load-dependent relaxation in the intact dog heart. Circ Res 1981;48:813–24.
6. Martin G, Gimeno JV, Cosin J, Guillem MI. Time constant of isovolumic pressure fall: new numerical approaches and significance. Am J Physiol 1984;247:H283–94.
7. Gaasch WH, Carroll JD, Blaustein AS, Bing OHL. Myocardial relaxation: effects of preload on the time course of isovolumetric relaxation. Circulation 1986;73:1037–41.
8. Hirota Y. A clinical study of left ventricular relaxation. Circulation 1980;62:756–63.
9. Thompson DS, Waldron CB, Juul SM, et al. Analysis of left ventricular pressure during isovolumic relaxation in coronary artery disease. Circulation 1982;65:690–7.
10. Gaasch WH, Blaustein AS, Bing OHL. Asynchronous (segmental early) relaxation of the left ventricle. J Am Coll Cardiol 1985;5:891–7.
11. Blaustein AS, Gaasch WH. Myocardial relaxation. VI. Effects of beta-adrenergic tone and asynchrony on LV relaxation rate. Am J Physiol 1983:244:H417–22.
12. Heyndrickx GR, Vantrimpont PJ, Rousseau MF, Pouleur H. Effects of asynchrony on myocardial relaxation at rest and during exercise in conscious dogs. Am J Physiol 1988;254:H817–22.
13. Zile MR, Blaustein AS, Shimizu G, Gaasch WH. Right ventricular pacing reduces the rate of left ventricular relaxation and filling. J Am Coll Cardiol 1987;10:702–9.
14. Badke FR, Boinay P, Covell JW. Effects of ventricular pacing on regional ventricular performance in the dog. Am J Physiol 1980;238:H858–67.
15. Waldman LK, Covell JW. Effects of ventricular pacing on finite deformation in canine left ventricles. Am J Physiol 1987;252:H1023–30.
16. Raya TE, Gay RG, Lancaster L, Aguirre M, Moffett C, Goldman S. Serial changes in left ventricular relaxation and chamber stiffness after large myocardial infarction in rats. Circulation 1988;77:1424–31.
17. Wynne J, Green LH, Mann T, Levin D, Grossman W. Estimation of left ventricular volumes in man from biplane cineangiograms filmed in oblique projections. Am J Cardiol 1978;41:726–32.
18. Yamamoto K, Kodama K, Hirayama A, et al. The effect of atrial contraction and synchroneity of cardiac contraction on ventriculo-arterial coupling (abstr). J Am Coll Cardiol 1989;13(suppl A):206A.
19. Videen JS, Huang SK, Bazgan ID, Mechling E, Patton DD. Hemodynamic comparison of ventricular pacing and atrial synchronous ventricular pacing using radionuclide ventriculography. Am J Cardiol 1986;57: 1305–8.
20. Sowton E. Artificial pacing and sinus rhythm. Br Heart J 1965;27:311–8.
21. Kruse I, Arnman K, Conradson TB, Ryden L. A comparison of acute and long-term hemodynamic effects of ventricular inhibited and atrial synchronous ventricular inhibited pacing. Circulation 1982;65:846–85.
22. Ogawa S, Dreifus L, Shenoy P, Brockman S, Berkovits B. Hemodynamic consequences of atrioventricular and ventriculoatrial pacing. PACE 1978; 1:8–12.

23. Kruse I, Ryden L. A comparison of physical work capacity and systolic intervals with ventricular inhibited and atrial synchronous inhibited pacing. Br Heart J 1981;46:129–36.

24. Kristensson BE, Arnman K, Smedgard P, Ryden L. Physiological versus single-rate ventricular pacing: a double-blind cross-over study. PACE 1985;8:73–84.

25. Askenazi J, Alexander JH, Koenigsberg DI, Belic N, Lesch M. Alterations of left ventricular performance by left bundle branch block simulated with atrioventricular pacing. Am J Cardiol 1984;53:99–104.

26. Samet P, Castillo C, Bernstein WH. Hemodynamic consequences of sequential atrioventricular pacing. Subjects with normal hearts. Am J Cardiol 1968;21:207–11.

27. Zhou JT, Yu GY. Hemodynamic findings during sinus rhythm, atrial and AV sequential pacing compared to ventricular pacing in a dog model. PACE 1987;10:118–24.

28. Walsh RA, O'Rourke RA. Hemodynamic effects of cardiac pacing. In Varriale P, Naclerio EA, eds. Cardiac Pacing: A Concise Guide to Clinical Practice. Philadelphia: Lea & Febiger, 1979:123–31.

29. Grover M, Glantz SA. Endocardial pacing site affects left ventricular end-diastolic volume and performance in the intact anesthetized dog. Circ Res 1983;53:72–5.

30. Burkhoff D, Sagawa K. Influence of pacing site on canine left ventricular force-interval relationship. Am J Physiol 1986;250:H414–8.

31. Burkhoff D, Oikawa RY, Sagawa K. Influence of pacing site on canine left ventricular contraction. Am J Physiol 1986;251:H428–35.

32. Wiggers CJ. The muscular reactions of the mammalian ventricles to artificial surface stimuli. Am J Physiol 1925;73:346–78.

33. Rosenqvist M, Obel IWP. Atrial pacing and the risk for AV block: is there a time for change in attitude? PACE 1989;12:97–101.

34. Feruglio GA, Rickards AF, Steinbach K, Feldman S, Parsonnet V. Cardiac pacing in the world: a survey of the state of the art in 1986. PACE 1987;10:768–87.

35. Rosenqvist M, Brandt J, Schuller H. Long-term pacing in sinus node disease: effects of stimulation mode on cardiovascular morbidity and mortality. Am Heart J 1988;116:16–22.

36. Rosenqvist M, Brandt J, Schuller H. Atrial versus ventricular pacing in sinus node disease: a treatment comparison study. Am Heart J 1986;111: 292–7.

37. Bernstein SB, Van Natta BE, Ellestad MH. Experiences with atrial pacing. Am J Cardiol 1988;61:113–6.

38. Craig WE, Murgo JP, Pasipoularides A. Evaluation of time course of left ventricular isovolumic relaxation in humans. In: Ref 2:125–32.

39. Lew WYW, Rasmussen CM. Influence of nonuniformity on rate of left ventricular pressure fall in the dog. Am J Physiol 1989;256:H222–32.